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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/468,647	12/21/1999	ROBERT D. GORDON	B0192/7011	3881

7590 06/10/2002

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EXAMINER	
ANDRES, JANET L	
ART UNIT	**PAPER NUMBER**
1646	16

DATE MAILED: 06/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/468,647	GORDON ET AL.	
	Examiner	Art Unit	
	Janet L Andres	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-72* is/are pending in the application.

4a) Of the above claim(s) *5,8-10,13,16-20,22-29,32-38,48-53 and 57-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,11,12,15,21,30,31,39-47,54,56 and 72* is/are rejected.

7)☒ Claim(s) *43 and 72* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO AMENDMENT

1. Applicant's amendment filed 2 April 2002 is acknowledged. Claims 1-13 and 15-72 are pending in this application. Claims 5, 8-10, 13, 16-20, 22-29, 32-38, 48-53, and 57-71 are withdrawn from consideration as drawn to non-elected inventions.

The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

2. The certified copy of Applicant's foreign priority document has been received.

3. The information disclosure statement filed 9 February 2001 has been considered in full.

4. The objection to the specification and to claims 1-4, 6, 7, 11, 12, 15, 21, 30, 31, 39-44, and 54-56 is withdrawn in response to Applicant's amendment and argument with respect to claim 42.

5. The rejection of claims 1-4, 6, 7, 30, 39-43, 54-56, and 72 under 35 U.S.C. 101 is withdrawn in response to Applicant's amendment.

6. The rejection of claims 1-4, 6, 7, 11, 12, 15, 21, 30, 31, 39-47, 54-56, and 72 under 35 U.S.C. 112, first paragraph, as lacking written description is withdrawn in response to Applicant's amendment.

7. The rejection of claims 1-3, 6, 7, 11, 12, 15, 21, 30, 31, 39-41, and 44 under 35 U.S.C. 112, second paragraph, is withdrawn in response to Applicant's amendment.

Rejections/Objections Maintained/New Grounds of Rejection

8. The objection to claims 43 and 72 is maintained for reasons of record in the office action of paper no. 12. The claims still refer to a figure, rather than the identification numbers of entered sequences.

9. The rejection of claims 1-4, 6, 7, 11, 12, 15, 21, 30, 31, 39-47, 54-56, and 72 under 35 U.S.C. 112, first paragraph, as lacking enablement commensurate with the scope of the claims is maintained.

Applicant argues that the Examiner's arguments are not relevant when the "plain language" of the claims is considered. Applicant further argues extensive experimentation need not be undue if it is routine or if a reasonable amount of guidance is provided. Applicant further argues that not all of the Wands factors were considered. Applicant specifies 3), the presence or absence of working examples, 4) the nature of the invention, 5), the state of the prior art, 6) the relative skill of those in the art, 7), the predictability or unpredictability of success, and 8) the breadth of the claims.

Applicant's arguments have been fully considered but have not been found to be persuasive. While the claims have been amended, the "plain language" still includes sequences of only 70% homology, sequences comprising portions, and, for claim 30, sequences comprising small primers. Thus the claims still encompass molecules of very different structures. Applicant argues that one of skill in the art could readily identify VEGFX molecules using primers, as Applicant has done. However, as stated in the office action of paper no. 12, to assay a large number of molecules that might potentially encode functional proteins is not routine when the expectation of success is unpredictable. It is the inability to predict, based on the guidance in the

specification and in the prior art, which molecules will be useful that renders the amount of experimentation undue.

Applicant argues that a polypeptide incorporating the CUB domain would function in the same way as a CUB domain, as an inhibitor. However, as was stated on pages 2 and 3 of the office action of paper no. 12, since the CUB domain is inhibitory, but was derived from a stimulatory molecule, one of skill could not readily predict the function of sequences comprising such domains: Applicant's own teachings indicate VEGFX, which includes this domain, is stimulatory. Further, U.S. patent 6391311, which discloses a polypeptide identical to that described by Applicant (see below) recites different CUB domains from that described by Applicant: see column 3, line 49.

Applicant argues that the VEGF domain was identified by comparison with other VEGFs and that tests or procedures to verify the functional characteristics are known to those skilled in the art. However, while the procedures are known, the outcome is not, and it would not be routine experimentation to establish the activity of Applicant's invention when Applicant has been unable to do so.

Applicant states that the nature of the invention itself is such as to be readily understandable. Applicant argues that the state of the art in 1999 was such that one of skill could readily isolate, for example, splice variants. However, what is claimed is not splice variants or molecules with small variations, but, as set forth above, sequences that have only limited homology to that which Applicant has disclosed.

Applicant further argues that the level of skill in the art is high and that the required methods are known. Applicant additionally argues that the predictability of the art is high.

However, while the required methods are in fact known, standard, and reliable, their success in identifying molecules that encode functional VEGFX or CUB domains is not predictable. As stated above, as written, the claims encompass molecules comprising primers, as in claim 30, molecules of only 70% homology to the claimed invention, and sequences comprising inhibitory regions, as well as sequences encompassing a region that Applicant has not shown to be functional. Since changes of even a single amino acid can alter function, and since Applicant's claims encompass molecules of potentially very different sequences, one of skill in the art could not readily predict what activity, if any, molecules identified by art-standard methods and potentially within the scope of the claims would have. Thus, as stated on p. 5 of the previous office action, one of skill in the art would require additional guidance, such as information as to what structures would conserve CUB function and what structures would alter it, and information as to what features were necessary for the particular characteristics of VEGFX, in order to predictably practice Applicant's invention as broadly claimed.

10. The rejection of claims 4, 42, 43, 45-47, 54, 55, and 72 under 35 U.S.C. 112, second paragraph, is maintained.

Claims 43 and 72 still refer to a figure, as discussed in paragraph 8 above and on p. 7 of the office action of paper no. 12. Claim 4 recites "high stringency conditions", which are not defined on p. 5; only examples are provided. Claim 42 is drawn to the polynucleotide sequence of SEQ ID NO: 29. SEQ ID NO: 29 is an amino acid sequence. Claims 43-47 refer to SEQ ID NO: 30, which does not exist. Claims 54 and 55 appear to require a polynucleotide that encodes a polynucleotide.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

12. Claims 1-4, 6, 7, 11, 12, 15, 21, 30, 31, 39-47, 54-56, and 72 are newly rejected under 35 U.S.C. 102(e) as being anticipated by U.S. patent 6391311 (Ferrara et al., 2002, filed 17 March 1998).

The '311 patent teaches VEGF E. SEQ ID NO: 1 of this patent includes a region, positions 259-1293, that is identical to Applicant's SEQ ID NO: 3. This region is particularly pointed to as the coding region of VEGF E in column 3, line 39, of the patent. The translated amino acid sequence, SEQ ID NO: 2, is identical to SEQ ID NO: 2 of the instant application. Thus the '311 patent anticipates sequences encoding SEQ ID NO: 2 and sequences comprising

portions of the sequence identified by Applicant as VEGFX. In addition, histidine-tagged molecules, as in instant claims 40 and 41, are taught in column 11, lines 48-50.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 872-9306 or (703) 872-9307 for after final communications.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to **[yvonne.eyler@uspto.gov]**.

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.
June 5, 2002

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER